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PTO/SB/05 (1/98) A

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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	787446-2001.1
First Inventor or Application Identifier	SCOTT E. PETERS, DARRYL H. WOODS
Title	A STABLE AQUEOUS DISPERSION OF NUTRIENTS
Express Mail Label No.	EL250497861US

APPLICATION ELEMENTS
See MPEP chapter 600 concerning utility patent application contents.

ADDRESS TO: **Assistant Commissioner for Patents, Box Patent Application, Washington, DC 20231**

1. ☒ * Fee Transmittal Form (e.g., PTO/SB/17) *(Submit an original, and a duplicate for fee processing)*
2. ☒ Specification [Total Pages 12]

(preferred arrangement set forth below, MPEP 1503.01)
- Descriptive title of the Invention
- Cross References to Related Applications
- Statement Regarding Fed sponsored R & D
- Reference to Microfiche Appendix
- Background of the Invention
- Brief Summary of the Invention
- Brief Description of the Drawings *(if filed)*
- Detailed Description,
- Claim(s) (13)
- Abstract of the Disclosure (1 page)

3. ☐ Drawing(s)(37 CFR. § 1.152) [Total Sheets]
4. Oath or Declaration [Total Pages]
   a. ☐ Newly executed (original or copy) **(to follow)**
   b. ☐ Copy from a prior application (37 C.F.R. § 1.63(d)) *(for continuation/divisional with Box 17 completed)* **[Note Box 5 below]**
      i. ☐ DELETION OF INVENTOR(S) Signed statement attached deleting inventor(s) named in the prior application, see 37 C.F.R. §§ 1.63(d)(2) and 1.33(b).
5. ☐ Incorporation By Reference *(useable if Box 4b is checked)* The entire disclosure of the prior application, from which a Copy of the oath or declaration is supplied under Box 4b, is Considered to be part of the disclosure of the accompanying Application and is hereby incorporated by reference therein.
6. ☐ Microfiche Computer Program *(Appendix)*
7. Nucleotide and/or Amino Acid Sequence Submission *(if applicable, all necessary)*
   a. ☐ Computer Readable Copy
   b. ☐ Paper Copy (identical to computer copy)
   c. ☐ Statement verifying identity of above copies

JC922 U.S. PTO 09/685366 10/10/00

ACCOMPANYING APPLICATION PARTS

8. ☐ Assignment Papers (cover sheet & documents(s))
9. ☐ 37 C.F.R. § 3.73(b) Statement ☐ Power of Attorney *(when there is an assignee)*
10. ☐ English Translation Document *(if applicable)*
11. ☐ Information Disclosure Statement (IDS)/PTO-1449 ☐ Copies of IDS Citations
12. ☐ Preliminary Amendment
13. ☒ Return Receipt Postcard (MPEP 503) *(Should be specifically itemized)*
14. ☐ * Small Entity Statements(s) **(to follow)** *(PTO/SB/09-12)* ☐ Statement filed in prior application, Status still proper and desired
15. ☐ Certified Copy of Priority Document(s) *(if foreign priority is claimed)*
16. ☐ Other: _____

* A new statement is required to be entitled to pay small entity fees, except where one has been filed in a prior application and is being relied upon.

17. If a **CONTINUING APPLICATION**, check appropriate box, and supply the requisite information below and in a preliminary amendment:
☐ Continuation ☐ Divisional ☐ Continuation-in-part (CIP) of prior application No.: _____
Prior application information: Examiner _____ Group/Art Unit: _____

16. CORRESPONDENCE ADDRESS

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Name (Print/Type)	**JEROME ROSENSTOCK**	Registration No. (Attorney/Agent)	25,456
Signature	Jerome Rosenstock	Date	October 10, 2000

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Box Patent Application, Washington, DC 20231

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FEE TRANSMITTAL

Patent fees are subject to annual revision on October 1
These are the fees effective October 1, 1997.
Small Entity payments must be supported by a small entity statement, otherwise large entity fees must be paid. See Forms PTO/SB/09-12.

TOTAL AMOUNT OF PAYMENT	($) 710.00

Complete if Known	
Application Number	Not yet assigned
Filing Date	Herewith
First Named Inventor	Scott E. Peters, Darryl E. Woods
Examiner Name	Not yet assigned
Group/Art Unit	Not yet assigned
Attorney Docket No.	787446-2001.1

METHOD OF PAYMENT

1. ☒ The Commissioner is hereby authorized to charge indicated fees and credit any over payments to.

Deposit Account Name	Frommer Lawrence & Haug LLP
Deposit Account Number	50-0320

☒ Charge any Additional Fee Required Under 37 CFR 1 16 and 1.17 ☐ Charge the Issue Fee Set in 37 CFR 1.18 at the Mailing of the Notice of Allowance

2. ☒ Payment Enclosed

☒ Check ☐ Money Order ☐ Other

FEE CALCULATION

1. BASIC FILING FEE

Large Fee Code	Entity Fee ($)	Small Fee Code	Entity Fee ($)	Fee Description	Fee Paid
101	710	201	355	Utility filing fee	710.00
106	320	206	160	Design filing fee	
107	490	207	245	Plant filing fee	
108	710	208	355	Reissue filing fee	
114	150	214	75	Provisional filing fee	
				SUBTOTAL (1)	710.00

2. EXTRA CLAIM FEES

			Extra Claim		Fee from below		Fee Paid
Total Claims	13	-20** =	0	X	18	=	0.00
Ind. Claims	2	-3** =	0	X	80	=	39.00
Multiple Dependent				X		=	

** or number previously paid, if greater; for reissues, see below

Large Fee Code	Entity Fee ($)	Small Fee Code	Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	80	202	40	Independent claims in excess of 3
104	270	204	135	Multiple dependent claim, if not paid
109	80	209	40	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent
107	490	207	245	Plant filing fee
				SUBTOTAL (2) ($)0.00

FEE CALCULATION

3. ADDITIONAL FEES

Large Fee Code	Entity Fee ($)	Small Fee Code	Entity Fee ($)	Fee Description	Fee Paid
105	130	205		Surcharge – late filing fee or oath	
127	50	227	25	Surcharge – late provisional filing fee or Cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request of reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	380	216	190	Extension for reply within second month	
117	870	217	435	Extension for reply within third month	
118	1,360	218	680	Extension for reply within fourth Month	
128	1,850	228	925	Extension for reply within fifth month	
119	300	219	150	Notice of Appeal	
120	300	220	150	Filing a brief in support of an appeal	
121	260	221	130	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use Proceeding	
140	110	240	55	Petition to revive – unavoidable	
141	1,210	241	605	Petition to revive- unintentional	
142	1,210	242	605	Utility issue fee (or reissue)	
143	430	243	215	Design issue fee	
144	580	244	290	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Petitions related to provisional Applications	
126	240	126	240	Submission of Information Disclosure Statement	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	760	246	380	Filing a submission after final rejection (37 CFR 1 129(a))	
149	760	249	380	For each additional invention to be examined (37 CFR 1 129(b))	
Other fee (specify)					
Other fee (specify)					
				SUBTOTAL (3)	($)

* Reduced by Basic Filing Fee

SUBMITTED BY				Complete (if applicable)	
Typed or Printed Name	JEROME ROSENSTOCK			Reg. Number	25,456
Signature	Jerome Rosenstock	Date	10/10/00	Deposit Account	50-0320

mia2813

PATENT
787446-2001.1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
APPLICATION FOR LETTERS PATENT

Docket No. 787446-2001.1

TITLE: **A STABLE AQUEOUS DISPERSION OF NUTRIENTS**

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kod1148

A STABLE AQUEOUS DISPERSION OF NUTRIENTS

This application claims priority from U.S. provisional application Serial No. 60/161,995 filed October 28, 1999, which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

This invention relates to a stable aqueous dispersion of nutrients, and more particularly, to a dispersion comprising an ingredient selected from (a) an isoflavone, (b) lycopene, (c) lutein, (d) a Coenzyme Q or (e) a mixture of the foregoing ingredients; and a stabilizer.

DESCRIPTION OF THE RELATED ART

Nutritional ingredients, such as an isoflavone, e.g. a soybean derived isoflavone, are currently available in tablets or other dry forms because heretofore they could not be satisfactorily dispersed in water. The nutritional ingredients, such as an isoflavone, lycopene, lutein, Coezyme Q's, are not ordinarily dispersable in aqueous systems because they are only slightly water or oil soluble.

These nutritional ingredients are desirable for use in beverages and cosmetics, in the form of aqueous dispersions or liposomes. For example, isoflavone is employed to treat humans to lower cholesterol, to treat solid tumors and angiogenic diseases. Additionally, it reduces bone calcium loss and is an antioxidant which can reduce free-radical damage to cells. Accordingly, a means for rendering these ingredients water dispersible is needed and desired.

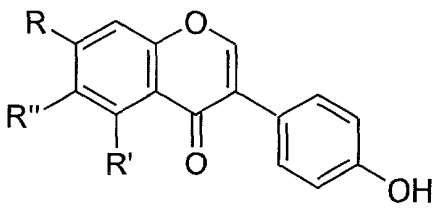
SUMMARY OF THE INVENTION

This invention relates to a stable suspension comprising a nutrient or nutritional ingredient and a stabilizer therefor dispersed in an aqueous system, e.g. a solvent comprising water. In particular, the ingredient is a nutrient selected from the group of (a) an isoflavone (b) lycopene, (c) lutein, (d) a Coenzyme Q_n, where n is an integer of 1 to 12, (e) a mixture of any of the foregoing ingredients.

DETAILED DESCRIPTION OF THE INVENTION

This invention involves a stable aqueous suspension which comprises a nutrient and a nutrient stabilizer dispersed in an aqueous system or solvent, e.g. water.

A suitable nutrient or nutritional ingredient is one which is suitable for therapeutic treatment of an animal, e.g. a human being, by ingestion, e.g. via a beverage, or a topical application, e.g. via a lotion or cream, but which is unfortunately typically insoluble or only slightly soluble in water at room temperature, e.g. 20°C to 25°C. It is these ingredients which are the subject of this invention. Some suitable nutrients or nutritional ingredients include (1) a compound of the formula,



where R is OH, β-glucoside, 6"-O-acetylglucoside, or 6"-O-malonylglucoside; R' is H or OH; and R" is H or OCH_3; such as isoflavone, e.g. a soybean derived isoflavone, and a substituted isoflavone, such as daidzein, genistein and glycitein; (2) lycopene, (3) lutein, (4) a Coenzyme Q_n,

where n is an integer of 1-12, e.g. Coenzyme Q_{10}, and (5) a mixture of any of the foregoing ingredients.

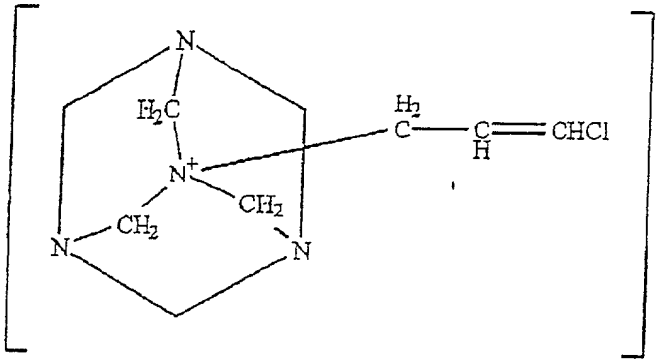
For purposes of the dispersions of this invention, which are intended for therapeutic use or as additives in association with therapeutic treatment of animals, e.g. a human, the particular nutrient or mixture of nutritional ingredients is present in the inventive aqueous dispersions in an effective nutritional amount, that is an amount which causes its desired nutritional or therapeutic effect.

The term "amount" as used herein refers to quantity or concentration as appropriate to the context. The amount of nutrient that constitutes a nutritional amount varies according to factors such as potency of the particular ingredient or mixture of ingredients, the route of administration and the mechanical system used to administer the dispersion. A nutritionally effective amount of a particular nutrient can be selected by those or ordinary skill in the art with due consideration of such factors. Generally, a nutritionally effective amount will be from .005 parts by weight to about 10 parts by weight based on 100 parts by weight of the dispersion.

A suitable aqueous system or medium is selected. A suitable aqueous system or medium for the dispersions of this invention include water and an aqueous solution of an organic alcohol of 1 to 6 carbon atoms, e.g. ethanol, propylene glycole, glycerine, etc., and a mixture of the foregoing; present in an amount of up to ten percent (10%) by weight. The aqueous system is one which will permit a stable dispersion to be formed therein when combined with the selected nutrient or mixture of nutrients, which in turn is destined to be combined with a suitable nutrient stabilizer. The aqueous system is present in an amount which affords the desired dispersion and is dependent upon the selected nutrient or mixture of nutritional ingredients with

the selected nutrient stabilizer. Typically, the aqueous system comprises 75 to 95 weight percent of the dispersion.

A suitable stabilizer is selected. A suitable stabilizer includes (1) a lecithin, derived from soybean or egg which contain a complex mixture of phospholipids consisting mainly of phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, and phosphatidic acid combined with varying amounts of other substances such as triglycerides; the lecithin can be of standard grade or can be modified or refined lecithin e.g. deoiled, hydrogenated, hydroxylated, enzyme modified, acetylated, etc.; (2) a hydrocolloid, e.g. xanthan gum, a pectin, gelatin, guar gum, carrageenan; (3) a surfactant, e.g. cetylpyridinlium chloride, polysorbate 80, sorbitan monostearate, polyglycerolesters, block copolymers of propylene oxide, ethylene oxide; (4) a Dowicil, a product of Dow Chemical Co., e.g. Dowicil 200 of the formula



; and

(5) a mixture of any of the foregoing stabilizers.

An aqueous dispersion of the selected nutrient comprises the nutrient stabilizer in an amount effective to stabilize the aqueous dispersion relative to an identical aqueous formulation or mixture not containing the nutrient stabilizer, such that the active ingredient does

not settle, cream or flocculate after agitation so quickly as to prevent reproducibility, e.g. reproducible dosing. Reproducible application, e.g. dosing, can be achieved if the resultant aqueous suspension is substantially uniform for about 1 to 2 hours after agitation thereof.

The particular amount of stabilizer that constitutes an effective amount is dependent upon the particular stabilizer, the particular aqueous system or medium employed and the particular nutritional ingredient or mixture of ingredients employed. It is therefore not practical to enumerate a specific effective amount for use with specific dispersions or formulations of the invention, but such amount can readily be determined by those skilled in the art with due consideration of the factors set forth above. Generally, however, the stabilizer can be present in a formulation in an amount from about 0.05 percent by weight to about 10 percent by weight, more preferably about .2 percent to about 5 percent by weight, based on the weight of the dispersion or formulation.

Typically, the nutrient stabilizer, e.g. Dowicil 200 preservative, is combined with the aqueous system, e.g. water, at a temperature of 20° to 70°C and is mixed for 2 to 10 minutes. Thereafter the active ingredient or nutritional agent, e.g. isoflavone, is added thereto to form a mixture. The resultant mixture is then subjected to a microfluidization treatment using any commercially available microfulidizer, e.g. Microfluidics M110, at a minimum shear pressure of 6500-7000 psi, preferably at a sheer pressure of 6500 to 8000 psi, and most preferably at a shear pressure of 7000 to 7500 psi, whereby a particle size to the active ingredient typically is less than 500nm, preferably less than 300 nm, most preferably less than 250 nm, to form the desired aqueous dispersion.

It is noted that the procedure described above can be modified, namely the stabilizer is added to the resultant aqueous dispersion, i.e. subsequent to the described microfluidization of the mixture of the nutrient combined with the aqueous system.

The resultant aqueous nutrient dispersion can then be further formulated and administered to a patient, e.g. a mammal such as a human being, by any conventional means, such as topically, orally; etc. Typically the dispersion is combined with other drugs, adjuvants, etc. in the form of a cream or lotion, e.g. a cosmetic, or in the form of a liquid, e. g. a beverage.

EXAMPLES

EXAMPLE 1:

SoyLife 100, a product manufactured by Schouten, Inc. 3300 Edinborough Way, Minneapolis, MN 55435, contains ten percent by weight of soy derived isoflavone. Ten weight percent of this material was mixed or dispersed with 0.2% by weight of Dowicil 200 and 89.8% by weight of water using a laboratory mixer. The resultant mixture was fluidized twice through a Microfluidizer (a product manufacture by MicroFluidics, Corp.) at 7,400-psi sheer pressure and 40 psi head pressure. The resultant slurry or dispersion was homogeneous and could easily be incorporated into a skin cream formulation.

EXAMPLE 2:

Prevastein HC, a product of Central Soya, 1946 West Cook Road, Fort Wayne, IN 46801, contains 40% by weight of isoflavone. Ten weight percent of this nutrient was combined with 0.1 percent by weight of potassium sorbate and 0.1% by weight of citric acid in 89.8% by weight of water. The resultant mixture was mixed with a laboratory mixer, then fluidized twice through the microfluidizer as in Example 1, at 7500-psi sheer. Rhodigel (xanthan

gum), 0.5% by weight, was added to the fluidized sample during high-speed mixing with a laboratory mixer. The resultant product was a thick viscous liquid that did not separate.

The resultant dispersion obtained in Example 2 was compared to samples prepared similarly to Example 2 but did not include a stabilizer and/or was not fluidized.

When diluting the dispersion prepared in Example 2 with water (0.25-0.5% dispersion), the nutrient remained dispersed for over a week, with very little precipitation forming. The other samples prepared were diluted at similar levels as the Example 2 sample, but these dispersions precipitated much more quickly (within 1-2 hours).

WE CLAIM:

1. A stable suspension comprising,

a nutrient selected from the group consisting of (a) an isoflavone, (b) lycopene, (c) lutein, (d) Coenzyme Q_n, were n is integer of 1 to 12; and (e) a mixture of any of the foregoing nutrients;

a nutrient stabilizer; and

an aqueous solvent system.

2. The suspension as defined in claim 1 where in said stabilizer is selected for the group consisting of (a') a lecithin, (b') a hydrocolloid, (c') a surfactant, (d') a Dowicil and (e') a mixture of any of the foregoing stabilizers.

3. The suspension as defined in claim 2 wherein said lecithin is selected from the group consisting of a lecithin derived from soybean or egg.

4. The suspension as defined in claim 2 wherein said hydrocolloid is selected from the group consisting of xanthan gum, a pectin, gelatin, guar gum, carrageenan, methylcelluloses, hydroxypropyl celluloses, gum arabic and a mixture of the foregoing hydrocolloids.

5. The suspension as defined in claim 2 wherein said surfactant is selected from the group consisting of cetylpyridinium chloride, polysorbate 80, sorbitan monostearate, a polyglycerol ester, a block copolymer of propylene oxide, ethylene oxide and a mixture of any of the foregoing surfactants.

6. The suspension as defined in claim 3 wherein said stabilizer comprises said Dowicil.

7. A method of making a stabilized aqueous suspension of a nutrient which comprises:

(a) combining the nutrient with an aqueous medium to form an aqueous mixture;

(b) combining a nutrient stabilizer with the nutrient; and

(c) microfluidizing said aqueous mixture before or after step (b), above, to form the stabilized aqueous suspension.

8. The method as defined in claim 7 wherein the nutrient is selected form the group consisting of (a) an isoflavone, (b) lycopene, (c) lutein, (d) Coenzyme Q_n, were n is integer of 1 to 12; and (d a mixture of any of the foregoing nutrients.

9. The method as defined in claim 7 wherein said nutrient stabilizer is selected from the group consisting of (a') a lecithin, (b') a hydrocolloid, (c') a surfactant, (d') a Dowicil and (e') a mixture of any of the foregoing stabilizers.

10. The method as defined in claim 9 wherein said lecithin is selected from the group consisting of a lecithin derived from soybean or egg.

11. The method as defined in claim 9 wherein said hydrocolloid is selected from the group consisting of xanthan gum, a pectin, gelatin, guar gum, carrageenan, a methylcellulose, an hydroxypropyl cellulose, gum arabic and a mixture of the foregoing hydrocollids.

12. The method as defined in claim 9 wherein said surfactant is selected from the group consisting of cetylpyridinium chloride, polysorbate 80, sorbitan monostearate, a polyglycerol ester, a block copolymer of propylene oxide, ethylene oxide and a mixture of any of the foregoing surfactants.

13. The method as defined in claim 9 wherein said stabilizer comprises said Dowicil.

ABSTRACT

This invention relates to a stable aqueous dispersion of nutrients and more particularly, to an aqueous dispersions of an active nutritional ingredient selected form (a) an isoflavone, (b) lycopene (c) lutein, (d) a Coenzyme Q_n where n is an integer of 1 to 12, or (e) a mixture of any of the foregoing nutrients.